15 March 2024
EMA/70104/2024
Human Medicines Division

List of centrally authorised products requiring a notification of a change for update of annexes

Parallel distributors are only required to inform the EMA of changes to the labelling or leaflet related to any update of the annexes of marketing authorisation once a year in their annual update application, except in cases related to safety or quality issues. The following table lists the centrally authorised products for which the EMA requires notifications of safety update before implementation.

Name	EU number	Date of communication	Rationale
Adrovance	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-marketing case reports and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (WS2467), which are available on the Agency's website**
Aldurazyme	All presentations	15/03/2024	To update section 4.2 of the SmPC in order to modify the administration instructions following the assessment of procedure PSUSA/00001830/202104 based on literature review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0085), which are available on the Agency's website.**
Alkindi	All presentations	15/02/2024	Update of section 4.2 of the SmPC in order to update posology recommendations in case of incomplete dosing. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0019), which are available on both the European Commission website and the Agency's website.**
Ameluz	All presentations	15/03/2024	Update of section sections 4.2, 4.4, 4.5, 4.8, 5.1 and 6.6 of the SmPC in order to include artificial daylight lamps as an additional light source for photodynamic therapy in combination with Ameluz for the treatment of actinic keratoses based on final results from non-clinical study PT-0042-A and literature (investigator-initiator trials). The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 14/12/2023 (II/0055), which are available on the Agency's website
Anoro Ellipta	All presentations	15/01/2024	Grouped application comprising two type II variations as follows: - Update of section 4.8 of the SmPC in order to remove the duplication of 'rash' from the list of adverse drug reactions (ADRs) with frequency uncommon to align with a similar change previously accepted as part of the renewal procedure of Rolufta Ellipta. - To include significant changes to sections 2, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.5 of the SmPC, sections 3, 4, 5, 7 and 11 of the labelling and sections 2, 3, 4, 5 and 6 of the package leaflet for the medicinal products Anoro and Laventair containing the active substances Umeclidinium Bromide and Vilanterol The package leaflet and labelling are updated accordingly. **Parallel distributors must use the annexes dated 09/11/2023 (WS2509/G), which are available on the Agency's website.**
Azacitidine Accord	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 04/01/2024 (IAIN/0018), which are available on the Agency's website.**
Azacitidine betapharm	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IAIN/0017), which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Azacitidine Mylan	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IAIN/0017), which are available on the Agency's website.**
Benepali	All presentations	15/01/2024	To update section 4.6 of the SmPC and section 2 of the package leaflet for the safety information on breast feeding following assessment of the same change for the reference product. Furthermore, the MAH updated section 5.1 of the SmPC to update the clinical study information and minor editorial changes, and section 2 of the package leaflet to align safety information for the users following assessment of the same change for the reference product. Update of section 4.8 of the SmPC to add Glomerulonephritis (frequency not known). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (PSUSA/00010795/202302 which also includes the IB/0079 scopes), which are available on the Agency's website.**
Benlysta	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to change the frequency of urticaria and rash from uncommon to common and to change the frequency of diarrhoea and nausea from very common to common and to update the Summary of the safety profile based on a cumulative review of clinical trials. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0117 which includes the II/0118 safety updates too), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
BESPONSA	All presentations	15/03/2024	Update of sections 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information based on final results from studies ITCC-059 (WI203581) and INO-Ped-ALL-1 (WI235086). Study WI203581 is a Phase 1/2, multicenter, European, multi-cohort, open-label study in pediatric patients (≥1 and <18 years of age) with R/R CD22-positive Acute Lymphoblastic Leukemia (ALL); and study WI235086 is an open-label, multi-center Phase 1 study to assess safety and tolerability of InO in Japanese pediatric patients with R/R CD22-positive ALL. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/12/2023 (II/0026), which are available on the Agency's website.**
Bimzelx	All presentations	15/01/2024	To correct the numbers in section 4.8 elderly patients (> 65 years). During the extension of indication - PsA (procedure no: EMEA/H/C/005316/II/0011), day 150 assessment; wrong numbers were transferred from the clinical documents to the SmPC and assessment report (EMA/CHMP/140126/2023). In addition, the applicant takes this opportunity to correct some formatting issues in the SmPC. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2023 (IB/0022), which are available on the Agency's website.**
Binocrit	All presentations	15/01/2024	Update of section 4.4 of the SmPC in order to allow for iron supplementation in accordance with patient needs and up-to date treatment guidelines by removing the restrictions to exclusively use the oral route of administration for iron supplementation. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI, bring it in line with the latest QRD template version 10.3, align it with the reference product and update instructions for use.

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			Parallel distributors must use the annexes dated 20/11/2023 (N/0107 which also includes the WS2534 scopes), which are available on the Agency's website.
Brukinsa	All presentations	15/01/2024	Extension of indication to include in combination with obinutuzumab treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic treatments for BRUKINSA; based on results from studies BGB-3111-212 and BGB-3111-GA101-001. BGB-3111-212 is an ongoing international, Phase 2, open-label, randomized (2:1), active control study of zanubrutinib plus obinutuzumab (Arm A) versus obinutuzumab monotherapy (Arm B) in patients with R/R FL. The primary efficacy endpoint is overall response rate (ORR); while BGB-3111-GA101-001 is a Phase 1b Study to Assess Safety, Tolerability and Antitumor Activity of the Combination of BGB-3111 with Obinutuzumab in Subjects with B-Cell Lymphoid Malignanciesa. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 15/11/2023 (II/0014), which are available on both the European Commission website and the Agency's website.**
Clopidogrel Teva	All presentations	15/03/2024	To update the below listed sections of the SmPC following assessment of the same for the reference product, Plavix: Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence, section 4.1, 4.2 and 5.1 of the SmPC is updated. To update the below listed sections of the SmPC and PL following assessment of the same for the reference product, Plavix: - Update of section 4.4 of the SmPC in order to update an existing

Name	EU number	Date of communication	Rationale
			warning on 'Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (IB/0059/G), which are available on both the European Commission website and the Agency's website.**
Dynastat	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to update skin reactions information based on literature and post-marketing data. pdate of section 4.6 of the SmPC to amend the available data on use during pregnancy, based on the PRAC advice for non-steroidal anti-inflammatory drugs (NSAID)-containing medicinal products (EMA/CMDh/642745/2022). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0088 which includes the PSUSA/00002314/202303 too), which are available on the Agency website.**
Enbrel	All presentations	15/01/2024	To update the instructions for use in section 7 of the package leaflet for 25 mg & 50 mg solution for injection in pre-filled pen (PFP). In addition, the MAH took the opportunity to update the PI with below editorial changes. 1. To update Labeling components (Packaging carton, labeling, package leaflet) for all Enbrel presentations with the new Pfizer Helix Logo. 2. To update Section 6 of the labelling (Annex IIIA - Minimum particulars to appear on small immediate packaging) by removing the reference of `pre-filled pen' to align with approved mock-ups of 25 mg and 50 mg PFP. 3. To update the address of the manufacturer responsible for batch release. Update of section 4.8 of the SmPC to add Glomerulonephritis (frequency not known). The package leaflet is updated accordingly.

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			Parallel distributors must use the annexes dated 14/12/2023 (PSUSA/00010795/202302 which includes the IB/0253 scopes), which are available on both the European Commission and the Agency's website.
Erelzi	All presentations	15/02/2024	Update of section 4.8 of the SmPC to add Glomerulonephritis with frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (PSUSA/10795/202302), which are available on both the European Commission website and the Agency's website.**
Erleada	All presentations	15/01/2024	Update of section 4.4 of the SmPC to add a warning regarding interstitial lung disease. Update of section 4.8 of the SmPC to add the adverse drug reaction "restless legs syndrome" (RLS) with a frequency "uncommon" and add the adverse reaction" interstitial lung disease" with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (PSUSA/00010745/202302), which are available on both the European Commission and the Agency's website.**
Fosavance	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-marketing case reports and literature. The package leaflet is updated accordingly.

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			Parallel distributors must use the annexes dated 30/11/2023 (WS2467), which are available on the Agency's website.
Glivec	All presentations	15/01/2024	Submission of the final report from study CSTI571I2201 - A European observational registry collecting efficacy and safety data in newly diagnosed pediatric Ph+ ALL patients treated with chemotherapy + imatinib ± HSCT, listed as an obligation in the Annex II of the PI. This study has been designed as an observational, multi-center registry to collect efficacy and safety data in Ph+ ALL pediatric patients (ages 1 to <18 years old) treated with chemotherapy + imatinib, with or without (± HSCT) primarily in European countries. The Annex II and the RMP (version 13.0_ and the package leaflet are updated accordingly. **Parallel distributors must use the annexes dated 31/08/2023 (II/0133), which are available on the Agency's website.**
Grepid	All presentations	15/02/2024	To update sections 4.1, 4.2, 4.4 and 5.1 of the SmPC to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI). To update sections 4.4 and 4.8 of the SmPC in order to update an existing warning on`Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (IB/0057/G), which are available on both the European Commission and the Agency's website.**
Imfinzi	All presentations	15/03/2024	Update of sections 4.2, 4.4 and 4.8 of the SmPC to add the adverse reactions of 'uveitis' and 'arthritis', a warning/precaution regarding these adverse reactions, and recommendations for treatment modifications when these adverse

Name	EU number	Date of communication	Rationale
			reactions occur. The package leaflet is updated accordingly. Update of section 4.4. of the SmPC to add a warning regarding patients with pre-existing autoimmune disease **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00010723/202304), which are available on the European Commission website.**
HyQvia	All presentations	15/02/2024	Extension of indication to include treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg in adults, children and adolescents for HyQvia. As a consequence, sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and labelling are updated in accordance. **Parallel distributors must use the annexes dated 25/01/2024 (II/0087), which are available on the European Commission website.**
Imfinzi	All presentations	15/01/2024	Extension of indication to include IMFINZI as treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from study D419CC00002 (HIMALAYA); this was a randomized, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma (HIMALAYA). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 15/11/2023 (II/0057), which are available on the European Commission website.**
Imraldi	All presentations	15/02/2024	To update section 3 of the SmPC to add "opalescent" and "pale brown" to the pharmaceutical form description. The package leaflet has been updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 23/01/2024 (IB/0070), which are available on the Agency's website.
Increlex	All presentations	15/02/2024	Update of sections 4.2, 4.6, and 4.8 of the SmPC in order to modify administration instructions recommendation regarding the monitoring of pre-prandial blood glucose in pre-prandial condition and in case of symptoms and to prevent the risk of lipohypertrophy, delete wording in the pregnancy section and update on number of patients with severe primary IGFD based on the cumulative review of safety database, scientific literature and clinical trials data. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/10/2023 (II/0080), which are available on the Agency's website.**
Incruse Ellipta	All presentations	15/02/2024	Update of sections 4.2, 4.6 and 4.8 of the SmPC to add 'Dysphonia' and 'Oropharyngeal pain' to the list of adverse drug reactions (ADRs) with frequency rare, and to update the wording regarding the administration instructions and for pregnancy and breast-feeding. ***Both the package leaflet and the labelling are updated accordingly.*** **Parallel distributors must use the annexes dated 14/12/2023 (WS2485), which are available on the Agency's website.**
Inovelon	All presentations	15/01/2024	Update the SmPC, labelling and package leaflet with excipient warnings for benzoic acid, sorbitol and sodium as per the Guideline (and Annex) on `Excipients in the labelling and package leaflet of medicines for human use', without any impact on the content of the dossier. In addition, the MAH has taken the opportunity to remove the word "rare" in relation to sorbitol wording for clarity of meaning. Furthermore, the MAH has taken the opportunity to correct the list of ingredients for Simethicone emulsion 30%, for Oral Suspension in section 6.1 of the SmPC and

Name	EU number	Date of communication	Rationale
			section 6 of the package leaflet to align with the current Agency approved dossier, as an editorial change. Lastly, the MAH has taken the opportunity to update E-numbers in sections 2 and 6.1 of the SmPC and in section 6 of the package leaflet, where applicable as per commission regulation (EU) No 231/2012. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 28/11/2023 (IB/0067), which are available on the Agency's website.**
Jardiance	All presentations	15/01/2024	Extension of indication for JARDIANCE to include treatment of children aged 10 years and above with type 2 diabetes based on results from study DINAMO 1218-0091; this is a double-blind, randomised, placebo-controlled, parallel group trial to evaluate the efficacy and safety of empagliflozin and linagliptin over 26 weeks, with a double-blind active treatment safety extension period up to 52 weeks, in children and adolescents with type 2 diabetes mellitus. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 07/12/2023 (II/0076), which are available on the European Commission website.**
Jemperli	All presentations	15/01/2024	Extension of indication to include in combination with platinum-containing chemotherapy the treatment of adult patients with mismatch repair deficient (dMMR)/ microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy, based on results from study 213361 (RUBY) Part 1, listed as a Specific Obligation in the Annex II; this is a phase 3, randomized, double-blind, multicenter study of dostarlimab (TSR-042) plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel in patients with recurrent or primary advanced endometrial cancer. As a consequence, sections

Name	EU number	Date of communication	Rationale
			4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and package leaflet are updated in accordance. **Parallel distributors must use the annexes dated 07/12/2023 (II/0023), which are available on both the European Commission and the Agency's website**
Kaftrio	All presentations	15/03/2024	To update Sections 4.2, 4.4, and 4.8 of the SmPC to emphasise the warning about the risk of drug induced elevated transaminases as requested in Article 46 WS procedures EMEA/H/C/005269/P46/013 and EMEA/H/C/005269/P46/014. Update of section 4.6 of the SmPC to amend the wording regarding breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00010868/202304 which also includes the IB/0045 scopes), on both the European Commission and the Agency's website**
Kalydeco	All presentations	15/01/2024	Update of sections 4.4 and 4.8 of the SmPC to add a warning regarding depression and to add the adverse reaction depression with a frequency "not known". Update of section 4.6 of the SmPC to amend the wording regarding breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/12/2023 (PSUSA/00009204/202301), which are available on the European Commission website.**
Kesimpta	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on injection-related reactions and to add 'Hypersensitivity reactions' to the list of adverse drug reactions (ADRs) with frequency not known. The package leaflet is updated accordingly. Addition of a statement in the pre-filled syringes (PFS) instructions for use when

Name	EU number	Date of communication	Rationale
			PFS has been dropped on a hard surface. The instructions for use have been updated accordingly. **Parallel distributors must use the annexes dated 09/02/2024 (II/0006) which are available on the Agency's website.**
Keytruda	All presentations	15/01/2024	Extension of indication to include KEYTRUDA in combination with gemcitabine and cisplatin for the first-line treatment of locally advanced unresectable or metastatic biliary tract carcinoma in adults, based on final results from study KEYNOTE-966; this is a Phase 3 randomized, double blind study of Pembrolizumab plus Gemcitabine/Cisplatin versus Placebo plus Gemcitabine/Cisplatin as first-line therapy in participants with advanced and/or unresectable biliary tract carcinoma. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. Extension of indication to include in combination with chemotherapy the first-line treatment of locally advanced unresectable or metastatic HER2-negative gastric or gastrooesophageal junction adenocarcinoma in adults whose tumours express PD L1 with a CPS $\geq$ 1 based on study KEYNOTE-859, a randomised, double-blind phase 3 trial, evaluating KEYTRUDA in combination with chemotherapy compared to placebo in combination with chemotherapy for the first-line treatment of patients with HER2-negative locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (II/0138 which also includes the II/0135 scopes), which are available on both the European Commission website and the Agency's website.**

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Kivexa	All presentations	15/01/2024	Update of section 4.4 of the SmPC to add a warning/precaution regarding cardiovascular events. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2023 (PSUSA/00000011/202212), which are available on both the European Commission website and the Agency's website.**
Laventair Ellipta	All presentations	15/01/2024	Update of section 4.8 of the SmPC in order to remove the duplication of 'rash' from the list of adverse drug reactions (ADRs) with frequency uncommon to align with a similar change previously accepted as part of the renewal procedure of Rolufta Ellipta. - To include significant changes to sections 2, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.5 of the SmPC, sections 3, 4, 5, 7 and 11 of the labelling and sections 2, 3, 4, 5 and 6 of the package leaflet for the medicinal products containing the active substances Umeclidinium Bromide and Vilanterol The package leaflet and Labelling are updated accordingly. **Parallel distributors must use the annexes dated 09/11/2023 (WS2509/G) which are available on the Agency's website.**
Lenvima	All presentations	15/01/2024	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to update paediatric information based on final results from studies E7080-G000-207 and E7080-G000-230. Study E7080-G000-207 is a multicenter, open-label, Phase 1/2 study of lenvatinib in children and adolescents with refractory or relapsed solid malignancies and young adults with osteosarcoma; Study E7080-G000-230 is a multicenter, open-label, randomized Phase 2 study to compare the efficacy and safety of lenvatinib in combination with ifosfamide and etoposide versus ifosfamide and etoposide in children, adolescents and young adults with Relapsed or Refractory Osteosarcoma (OLIE). The package leaflet is updated accordingly. Submission of interim

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			results from study E7080-M000-508 (STELLAR), listed as a category 3 PASS in the RMP. This is a non-interventional multicentre, observational, phase 4 study to evaluate the safety and tolerability of lenvatinib in patients with advanced or unresectable HCC. Update of section 4.8 of the SmPC to include 'gastrointestinal perforation' as an adverse drug reaction with frequency 'common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (II/0053 which also includes the II/0050 scopes) which are available on the Agency's website.**
Lixiana	All presentations	15/01/2024	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with available paediatric data based on final results from study DU176b-D-U312; this is a phase 3, open-label, randomised, multicentre, controlled trial to evaluate the pharmacokinetics and pharmacodynamics of edoxaban and to compare the efficacy and safety of edoxaban with standard-of-care anticoagulant therapy in paediatric subjects from birth to less than 18 years of age with confirmed venous thromboembolism (VTE). In addition, the MAH took the opportunity to clarify that edoxaban tablets can be delivered through a nasogastric tube in Section 4.2 of the SmPC. The packagel and labelling are updated accordingly... **Parallel distributors must use the annexes dated 29/11/2023 (WS2409) which are available on the Agency's website**
Lokelma	All presentations	15/01/2024	Update of section 4.8 of the SmPC to include information on constipation to the summary of safety profile and to add constipation to the list of adverse drug reactions (ADRs) with frequency Common based on literature review and MAH safety database. The package leaflet is updated accordingly.

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			Parallel distributors must use the annexes dated 14/12/2023 (II/0033) which are available on the Agency's website
Lonquex	All presentations	15/01/2024	Update of section 4.4 of the SmPC in order to add a class-effect warning risk of Acute Myeloid Leukaemia and Myelodysplastic Syndrome in breast and lung cancer patients in conjunction with chemotherapy and/or radiotherapy based on the cumulative review of literature and MAH safety database. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/11/2023 (IA/0086 which includes the II/0080 scopes) which are available on the Agency's website**
Lopinavir/Ritonavir Mylan	All presentations	15/02/2024	To update section 4.5 of the SmPC to reflect an additional drug-drug interaction with dabigatran etexilate and edoxaban. The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 16/01/2024 (IB/0027) which are available on the Agency's website**
Lyrica	All presentations	15/01/2024	Update of section 4.4 and 4.8 of the SmPC to include suicidal ideation as part of the observed withdrawal symptoms. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (IG1690/G which includes the PSUSA/00002511/202301), which are available on the Agency's website.**
Mavenclad	All presentations	15/02/2024	Update of sections 4.5 and 4.6 of the SmPC to add information regarding the use of mavenclad with oral contraceptives based on the final study results from the drug-drug interaction study (MS 700568-0031). Annex II and the package leaflet are updated accordingly.

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			Parallel distributors must use the annexes dated 30/11/2023 (II/0027), which are available on the Agency's website.
Mayzent	All presentations	15/02/2024	Update of section 4.8 of the SmPC to amend the PML frequency from "unknown" to "rare". The package leaflet is updated accordingly. Update of section 4.4 of the SmPC to amend a warning regarding reduction in heart rate and atrioventricular conduction. **Parallel distributors must use the annexes dated 05/01/2024 (PSUSA/00010818/202303) which are available on the European Commission website.**
Mirapexin	All presentations	15/02/2024	Update of section(s) 4.2, 4.4 and 4.8 of the SmPC to highlight that the lowest effective dose should be used, amend the warning/precaution regarding restless legs augmentation syndrome and to add the adverse reaction restless legs augmentation syndrome with a frequency 'very common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/01/2024 (PSUSA/00002491/202304) which are available on the European Commission website.**
Mircera	All presentations	15/01/2024	To update the Product Information to update the Instrutions for Use (IFU) by giving additional information to the user to ensure the correct and safe usage of the needle. Furthermore, the Marketing Authorisation Holder has taken the opportunity to: - implement editorial changes in sections 4.4 (traceability) and 4.8. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/12/2023 (IB/0096), which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Mounjaro	All presentations	15/01/2024	Extension of indication to include chronic weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial body mass index (BMI) of ≥ 30 kg/m2 (obesity), or ≥ 27 kg/m2 to < 30 kg/m2 (overweight) in the presence of at least one weight-related comorbid condition, based on a global, pivotal phase 3 study I8F-MC-GPHK (SURMOUNT-1) and five supportive phase 3 studies (SURPASS-1 to -5) in participants with T2DM and BMI ≥ 27 kg/m2. SURMOUNT-1 is a phase 3, randomized, double-blind, placebo-controlled trial to investigate the efficacy and safety of tirzepatide once weekly in participants without type 2 diabetes who have obesity or are overweight with weight related comorbidities. As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. Update of section 4.8 of the SmPC in order to add 'anaphylactic reaction' and 'angioedema' to the list of adverse drug reactions (ADRs) with frequency rare, based on reviews of post-marketing safety data. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (II/0007 which includes the II/0010 too) which are available on the European Commission website.**
Moventig	All presentations	15/01/2024	Update of sections 4.2 and 4.4 of the SmPC based on real-world data from non-interventional studies (NACASY, KYONAL and MOVE studies), post-marketing data, and literature on the use of naloxegol in OIC patients with cancer-related pain. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (II/0039) which are available on both the European Commission and the Agency website.**

Name	EU number	Date of communication	Rationale
Myozyme	All presentations	15/03/2024	Update of section 4.2 of the SmPC in order to add home infusion upon request by PRAC following the assessment of PSUSA/00000086/202109 I based on a cumulative search of the MAH Global Pharmacovigilance database and literature. The Package Leaflet and Annex II are updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0094), which are available on the Agency's website.**
Nepexto	All presentations	15/01/2024	To update section 4.6 of the SmPC in order to update information on breast feeding exposure based on the cumulative review of etanercept specific pharmacology, safety database and published medical literature, following assessment of the same changes adopted for the parent product; section 5.1(Pharmacodynamics) of SmPC has been updated in line with reference product. Section 2 of the package leaflet is updated accordingly. In addition, the MAH introduced minor editorial changes to align to reference product. **Parallel distributors must use the annexes dated 19/12/2023 (IB/0027), which are available on the Agency's website.**
Neupro	All presentations	15/01/2024	Update of section 4.4 of the SmPC to add a warning regarding the possibility for Parkinson Disease patients to experience dystonic events. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (PSUSA/00002667/202302), which are available on the Agency's website**.
Nevanac	All presentations	15/03/2024	To remove from SmPC section 4.8 (undesirable effect) "Uncommon: hypertension" as blood pressure increase is listed in the annexes as well.To replace the statement "Rinse your eye out with warm water" with "Contact your doctor for detailed instruction" in the package leaflet section 3. In addition the MAH has updated the

Name	EU number	Date of communication	Rationale
			translations with minor linguistic correction and to comply with QRD. **Parallel distributors must use the annexes dated 28/02/2024 (IAIN/0055 which includes the IB/0054/G safety scopes), which are available on the Agency's website**
Ninlaro	All presentations	15/01/2024	Submission of the Clinical Study Report (Addendum 2) for study C16019 listed as a Specific Obligation in the Annex II of the Product Information. This is a phase 3, randomized, double-blind, placebo-controlled study of single-agent oral ixazomib as maintenance therapy following autologous stem cell transplant (ASCT) for patients with newly diagnosed multiple myeloma. In addition, the MAH proposes to remove NINLARO from the list of medicines subject to additional monitoring and to remove the black triangle from the SmPC. The Annex II and package leaflet are updated accordingly. **Parallel distributors must use the annexes dated 03/11/2023 (II/0045), which are available on both the European Commission website and the Agency's website.**
Ontozry	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC to amend /add information relating to suicidality following the use of cenobamate. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 12/01/2024 (PSUSA/00010921/202303), which are available on both the European Commission website and the Agency's website.**
Pravafenix	All presentations	15/01/2024	Update of section 4.8 of the SmPC to add the adverse reaction muscle rupture with a frequency "not known". The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 22/02/2024 (PSUSA/00001363/202304), which are available on the European Commission website.
Posaconazole Accord	All presentations	15/01/2024	Update sections 4.1, 4.2, 5.1 and 5.3 of the SmPC to extend the approved indications to the paediatric population for Posoconazole gastro-resistant tablets, following assessment of the same changes in the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (IB/0013), which are available on both the European Commission website and the Agency's website.**
Pradaxa	All presentations	15/01/2024	To delete the pharmaceutical form "powder and solvent for oral solution, 6.25 mg/ml", as agreed in procedure EMEA/H/C/000829/II/0144. Update of section 4.1 and 4.2 of the SmPC in order to modify the indication and posology following the deletion of the powder and solvent for oral solution formulation. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (II/0147/G) which are available on the European Commission website.**
Praluent	All presentations	15/01/2024	Extension of indication to include treatment of paediatric patients 8 years of age and older with heterozygous familial hypercholesterolemia (HeFH) as an adjunct to diet, alone or in combination with other LDL-C lowering therapies, based on final results from study EFC14643 listed as a category 3 study in the RMP; this is a randomized, double-blind, placebo-controlled study followed by an open-label treatment period to evaluate the efficacy and safety of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia. As a consequence,

Name	EU number	Date of communication	Rationale
			sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2023 (II/0078) which are available on both the European Commission website and the Agency's website.**
Pregabalin Pfizer	All presentations	15/01/2024	Update of section 4.4 and 4.8 of the SmPC to include suicidal ideation as part of the observed withdrawal symptoms. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (IG1690/G which includes the PSUSA/00002511/202301) which are available on the Agency's website.**
Prevymis	All presentations	15/01/2024	Extension of indication to include prophylaxis of CMV disease in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-], based on the final results from study P002MK8228; this is Phase III, Randomized, Double-Blind, Active Comparator- Controlled Study to Evaluate the Efficacy and Safety of MK-8228 (Letermovir) Versus Valganciclovir for the Prevention of Human Cytomegalovirus (CMV) Disease in Adult Kidney Transplant Recipients. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information. C.I.4: Update of section 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC to reflect a longer duration of treatment recommendation based on the final results from study P040MK8228; this is a Phase 3 randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of letermovir (LET) prophylaxis when extended from 100 days to 200 days post-transplant in

Name	EU number	Date of communication	Rationale
			cytomegalovirus (CMV) seropositive recipients (R+) of an allogeneic hematopoietic stem cell transplant (HSCT). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2023 (II/0033/G) which are available on the European Commission website**
Protopic	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend the warning/precaution recommending against use in patients with a skin barrier defect. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/02/2024 (PSUSA/00002840/202303) which are available on both the European Commission website and the Agency's website.**
Reblozyl	All presentations	15/03/2024	Submission of the final report from study ACE-536-MDS-005 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study (PASS) to evaluate the effectiveness of the additional risk minimisation measure (aRMM) for Reblozyl among Healthcare Providers (HCPs) in the EU/EEA. Update of section 4.6 of the PI and Annex II.D. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0023) which is available on the Agency's website.**
Remicade	All presentations	15/01/2024	To update section 4.8 of the SmPC to add weight increased to the list of adverse drug reactions (ADRs) with frequency Uncommon following PRAC PSUR assessment report (EMA/PRAC/158162/2023-Corr.1) based on the cumulative literature review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (II/0243) which is available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Retsevmo	All presentations	15/03/2024	Extension of indication to include the treatment of adults and adolescents 12 years and older with advanced RET fusion-positive thyroid cancer in the first-line setting for RETSEVMO based on interim data from studies LIBRETTO-001 (LOXO-RET-17001) and LIBRETTO-121; LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumors. LIBRETTO-121 is a Phase 1/2 study of selpercatinib in paediatric patients with advanced RET-altered solid or primary central nervous system tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 29/02/2024 (II/0021) which are available on both the European Commission website and the Agency's website.**
Rinvoq	All presentations	15/01/2024	Update of sections 4.4 of the SmPC to add a warning regarding hypoglycaemia in patients treated for diabetes. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/12/2023 (PSUSA/00010823/202302) which are available on both the European Commission website and the Agency's website.**
Ritonavir Mylan	All presentations	15/02/2024	To update section 4.5 in order to reflect additional Drug-Drug Interaction with dabigatran etexilate and edoxaban. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IB/0020/G) which is available on the Agency's website.**
Rivastigmine Actavis	All presentations	15/03/2024	To update sections 4.4 and 4.5 of the SmPC to strengthen the existing warning on QT prolongation based on post-marketing data and literature, following assessment of the same

Name	EU number	Date of communication	Rationale
			change for the reference product, Exelon. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/02/2024 (IB/0032) which is available on the Agency's website**
Ryeqo	All presentations	15/01/2024	Extension of indication to include symptomatic treatment of endometriosis for RYEQO in adult women of reproductive age with a history of previous medical or surgical treatment for their endometriosis, based on final results from studies MVT-601-3101 and MVT-601-3102 and final results up to 104 weeks from study MVT-601-3103. Studies 3101 and 3102 are pivotal, phase III, randomised, double-blind, placebo-controlled, safety and efficacy studies to evaluate relugolix with E2 and NETA as a combination therapy for pain associated with endometriosis. In the extension part all patients received relugolix combination therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were updated. Update of section 4.5 of the SmPC to update information regarding Drug-Drug Interaction based on final results of DDI studies MVT-601-54, MVT-601-55 and MVT-601-57. Study MVT-601-54 is a 2-part interventional open-label study to assess the potential effects of erythromycin on the PK of the 3 components of Ryeqo. Study MVT-601-55 is an interventional open label fixed single sequence cross-over study to assess whether a 6-hour dose separation is sufficient to mitigate absorption mediated increased exposure to relugolix and study MVT-601-057 is a 2-part study to assess the potential effect of relugolix on the PK of total dabigatran. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/10/2023 (II/0013/G) which are available on both the European Commission website and the Agency's website**

Name	EU number	Date of communication	Rationale
Shingrix	All presentations	15/01/2024	Update of section 4.5 of the SmPC in order to add drug-drug interaction information with COVID-19 mRNA-1273 booster vaccine, based on final results from study ZOSTER-091; this is a phase 3, randomized, open-label, controlled, multi-center clinical study to evaluate the immune response and safety of both herpes zoster subunit vaccine (HZ/su or Shingrix) in healthy adults aged 50 years and older, and the quadrivalent seasonal influenza vaccine (Flu D-QIV or Fluarix Quadrivalent) in healthy adults aged 18 years and older, when administered sequentially or co-administered with mRNA-1273 booster vaccination. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/10/2023 (II/0065) which are available on the Agency's website.**
Sifrol	All presentations	15/02/2024	Update of section(s) 4.2, 4.4 and 4.8 of the SmPC to highlight that the lowest effective dose should be used, amend the warning/precaution regarding restless legs augmentation syndrome and to add the adverse reaction restless legs augmentation syndrome with a frequency 'very common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/01/2024 (EMEA/H/C/PSUSA/00002491/202304) which are available on both the European Commission website and the Agency's website.**
Spectrila	All presentations	15/01/2024	Update of sections 4.4 and 4.6 of the SmPC in order to include the recommendations from the SWP regarding genotoxic medicinal products and contraception duration period; the package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/03/2023 (II/0032/G) which are available on the European Commission website.**

Name	EU number	Date of communication	Rationale
Symkevi	All presentations	15/01/2024	Update of sections 4.4 and 4.8 of the SmPC to add "depression" as an adverse drug reaction with a frequency not known and introduce a warning to inform prescribers about the risk of depression. The Package leaflet is updated accordingly. Update of section 4.6 of the SmPC to amend wording regarding breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (PSUSA/00010730/202302) which are available on both the European Commission and the Agency's website.**
Tecentriq	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding the risk of immune-related adverse reactions in patients with pre-existing autoimmune disease. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2024 (PSUSA/00010644/202305) which are available on both the European Commission and the Agency's website**
Tecfidera	All presentations	15/01/2024	Update of section 4.6 of the SmPC in order to update information on pregnancy based on results from study 109MS402 - Tecfidera (dimethyl fumarate) Pregnancy Exposure Registry, listed as a category 3 study in the RMP; This is an observational study and aims to address the safety concern of effects on pregnancy outcome and prospectively evaluates pregnancy outcomes in women with MS who were exposed to a Registry-specified Biogen MS product during the eligibility window for that product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/10/2023 (II/0082) which are available on the Agency's website.**
Tegsedi	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to modify the warning on liver monitoring and drug-induced liver injury and to add 'drug-

Name	EU number	Date of communication	Rationale
			induced liver injury' to the list of adverse drug reactions (ADRs) with frequency not known. Annex II and the package leaflet are updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (II/0038) which are available on the Agency's website.**
Teysuno	All presentations	15/02/2024	To update section 4.6 of the SmPC according to WP/NcWP recommendation on the duration of contraception following the end of treatment with a genotoxic drug. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/01/2024 (IB/0055) which are available on the Agency's website.**
Toviaz	All presentations	15/01/2024	Update of section 4.4 of the SmPC to amend an existing warning on angioedema and 4.8 of the SmPC in order to add hypoaesthesia oral to the list of adverse drug reactions (ADRs) with a frequency rare based on a cumulative review of safety database cases and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/10/2023 (II/0068) which are available on the Agency's website**
Triumeq	All presentations	15/01/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding the risk of cardiovascular events for Triumeq, as an abacavir containing product ,in view of the available data coming from the literature regarding abacavir and its possible relation with cardiovascular events (notably myocardial infarction) in patients treated with abacavir. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2023 (PSUSA/00010075/202301) which are available on both the European Commission and the Agency's website.**

Name	EU number	Date of communication	Rationale
Trizivir	All presentations	15/01/2024	Update of section 4.4 of the SmPC to add a warning/precaution regarding cardiovascular events. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2023 (PSUSA/00003144/202212) which are available on both the European Commission and the Agency's website.**
Truvada	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding Bone effects. Update of section 4.8 of the SmPC to add the adverse reaction bone mineral density decreased with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/1210/202304) which are available on both the European Commission and the Agency's website.**
Tysabri	All presentations	15/03/2024	Update of sections 4.2 and 4.4 of the SmPC to modify administration instructions and update educational guidance to enable the subcutaneous formulation to be administered outside a clinical setting by healthcare professionals based on the cumulative review of post marketing and clinical study data. The package leaflet and Annex IID are updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0136) which are available on the Agency's website.**
Vantavo	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-

Name	EU number	Date of communication	Rationale
			marketing case reports and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (WS2467) which are available on the Agency's website.**
Vaxelis	All presentations	15/01/2024	Update of section 4.5 in order to add drug-drug interaction information with meningococcal B conjugate vaccine based on final results from study OVG 2018/05 - Immunogenicity and reactogenicity of concomitantly administered hexavalent and group B meningococcal vaccines in infancy; this is an open-label, non-inferiority, randomized clinical trial that compared the immune response and assessed the safety of Vaxelis and control vaccine (Infanrix hexa) when co-administered with 4 component meningococcal B vaccine (4CMenB) along with other routine infant vaccines. Update of section 4.8 of the SmPC in order to add Extensive swelling of vaccinated limb to the list of adverse drug reactions (ADRs) with frequency rare and to update its description based on the cumulative review of clinical studies, literature and safety database. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/12/2023 (II/0134 which includes the II/0128 scopes too), which are available on the Agency's website.**
Verzenios	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to add a new warning on "arterial thromboembolic events", based on a safety review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2023 (II/0028) which are available on the Agency's website**
Vidaza	All presentations	15/01/2024	To update section 4.8 of the SmPC to include cutaneous vasculitis as an undesirable effect, following the PRAC recommendation adopted on 28 September 2023

Name	EU number	Date of communication	Rationale
			(EMA/PRAC/416575/2023; EPITT No 19929). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 06/12/2023 (IAIN/0059) which are available on the Agency's website.**
Viread	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding Bone effects. Update of section 4.8 of the SmPC to add the adverse reaction bone mineral density decreased with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00002892/202303) which are available on both the European Commission and the Agency's website**
Vipdomet	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vitamin B12 decrease or deficiency and to update the list of adverse drug reactions (ADRs) in accordance with the recent update of the PI for Glucophage, which is the reference label for the compound metformin, and following the request by MHRA on 20 June 2022 for all products containing metformin. **Parallel distributors must use the annexes dated 26/10/2023 (II/0044) which are available on the Agency's website.**
Xultophy	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to add Dizziness and Delayed gastric emptying to the list of adverse drug reactions (ADRs) with frequency common and unknown, respectively, based on the cumulative review of clinical studies data, post marketing data, class labels and biological plausibility. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (II/0050), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Yescarta	All presentations	15/03/2024	To update section 4.4 of the SmPC and section 2 of the PL to implement the signal recommendation on 'Axicabtagene ciloleucel - Progressive multifocal leukoencephalopathy (PML)' (EPITT no 19940), adopted at the 27-30 November 2023 PRAC meeting. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2024 (IAIN/0071), which are available on the Agency's website.**
Zavicefta	All presentations	15/03/2024	Update of section 4.4 of the SmPC with information regarding the fact that cases of Crohn's disease have been reported post-marketing. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0033), which are available on the Agency's website.**
Zaltrap	All presentations	15/02/2024	Update of section 4.6 of the SmPC in order to update information regarding the duration of contraceptive use after cessation of treatment. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (Yearly update which includes II/0070), which are available on the European Commission website.**
Ziagen	All presentations	15/01/2024	Update of section 4.4 of the SmPC to add a warning/precaution regarding cardiovascular events. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/01/2024 (IB/0127, which includes the PSUSA/00000010/202212 scopes too), which are available on the Agency's website.**
Zinforo	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to add 'Kounis Syndrome' to the list of adverse drug reactions (ADRs). The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 25/01/2024 (II/0063) which are available on both the European Commission and the Agency's website
Zinplava	All presentations	15/02/2024	Extension of indication to include treatment of the paediatric population (1 to 18 years of age) for ZINPLAVA, based on final results from study MK-6072-001 (MODIFY III) listed as a category 3 study in the RMP. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/01/2024 (II/0037), which are available on the European Commission website.**
Zyllt	All presentations	15/03/2024	To update the below listed sections of the SmPC and PL following assessment of the same for the reference product Plavix: - Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence section 4.1, 4.2 and 5.1 of the SmPC is updated. C.I.2.a - To update the below listed sections of the SmPC and the package leaflet following assessment of the same for the reference product Plavix: - Update of section 4.4 of the SmPC in order to update an existing warning on 'Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (IB/0045/G) which are available on both the European Commission and the Agency's website**

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